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REMARKS

Claims 3-33 and 35-50 are pending. Claims 32-50 were elected for prosecution. However, only claims 32-36 and 39-44 have been examined on the merits and thus, are the subject of this Response to the Office Action. Claim 34 has been cancelled without prejudice.

The Office Action raised the following issues:

(a) Claims 34-35, 41 and 42-44 were rejected as being purportedly indefinite under 35 U.S.C. § 112, ¶ 2;

(b) Claims 32-36 and 39-44 were rejected under the judicially created doctrine of obviousness-type double patenting; and

(c) Claims 32-36 and 39-43 were rejected under 35 U.S.C. § 103(a) as being purportedly unpatentable over U.S. Patent Nos. 4,774,958 ("Feinstein") or 4,089,800 ("Temple") in view of "Structure of hollow polystyrene microspheres: an SEM study," J. Microencapsulation, 1989 6:2:193-198 ("Ganguly"). Claims 32-36 and 39-44 were further rejected under this same combination in view of U.S. Patent No. 4,265,251 ("Tickner") as well as over the combination of U.S. Pat. No. 5,425,366 ("Reinhardt") in view of Ganguly and Tickner.

For reasons discussed below, Applicants respectfully traverse each of the rejections above and respectfully submit that the pending claims, as amended, are definite and patentable over the cited references.

A. Claims 34-35, 41 And 42-44 Are Definite

Claims 34-35, 41 and 42-44 were rejected under 35 U.S.C. § 112, ¶ 2 as being purportedly indefinite. Applicants respectfully traverse.

The Examiner objected to the terms "a few nanometers" and "several thousands of nanometers" in claim 34. Office Action, p. 3. However, claim 34 has been cancelled without

prejudice to expedite prosecution and not for any reasons related to patentability. Claim 35 has been amended to correct its dependency. No range of equivalents is surrendered as a result of this amendment. Thus, this issue is moot for claims 34 and 35.

The Examiner objected to claims 42 and 43 because they respectively recite "the broad recitation phospholipids and polyalkylene glycols, and the claim also recite 'lecithins' and 'polyethylene glycol' which is the narrower statement of the range/limitation." Office Action, p. 3. Applicants respectfully request removal of this objection, since for example, neither claim 42 nor claim 43 recite the term phospholipids or lecithins.

The Examiner objected to claim 41 based on the term "and the like" in line 2 of that claim. To expedite prosecution and not for any reasons related to patentability, claim 41 was amended to delete this term. No range of equivalents is surrendered as a result of this amendment. Thus, this issue is moot for claim 41.

The Examiner objected to claim 44 based on the term "freon". Applicants traverse and submit that the generic term "freon" is properly claimed:

1. The Term "Freon" Is Well Understood In The Art

Applicants use the term "freon" to refer to the family of fluorinated carbon-containing compounds which have a distinctive set of characteristics. This family is well known and understood to those skilled in the art. Declaration Of Richard Chambers[1], ¶ 5 (Exhibit 1). Thus, the term "freon" is not indefinite and withdrawal of this rejection is respectfully requested.

Additionally, the term "freon" is used to refer to specific compounds that were disclosed to the public. This is not a case where a term is indefinite because it refers to some proprietary

[1] This declaration was submitted during the prosecution of the related application no. 09/115,963, which is the reissue application of parent U.S. Pat. No. 5,413,774.

formula, secret process or unknown entity. The chemical structures of the freons were known and therefore this rejection should be withdrawn.

2. The United States Patent And Trademark Office Has Acknowledged That A Claim To Freon Is Proper

Furthermore, the United States Patent And Trademark Office ("USPTO") has recognized and acknowledged the propriety of using the term "freon" by issuing claims in more than eight hundred patents which use this term. (Exhibit 2). A few representative claims of some recent patents issued by the USPTO which claim freon are reproduced below for the Examiner's convenience (*emphasis* added):

> U.S. Pat. No. 6,300,369 - Hydroxy-kojic acid skin peel
> 37. The method of claim 36, wherein said degreaser is selected from the group consisting of alcohol, acetone, *freon* and chlorhexidine
>
> U.S. Pat. No. 6,282,943 - Apparatus and method for detecting substances
> 13. The apparatus of claim 12, wherein the substance is a gas selected from the group consisting of natural gas, methane, propane, carbon monoxide, hydrogen sulfide, ethane, butane, oxygen, and *freon*.
>
> U.S. Pat. No. 6,277,143 - Brain cooling apparatus and method for cooling the brain
> 5. The apparatus according to claim 4, wherein the compressed liquid is selected from the group consisting of carbon dioxide, *freon* and nitrogen.
>
> U.S. Pat. No. 6,276,158 - Heat exchange equipment
> 15. Heat exchange equipment according to claim 1, in which the heat exchange fluid comprises a *freon*.
>
> U.S. Pat. No. 6,123,523 - Gas-dispersion device
> 20. A method as defined in claim 18 wherein said gas is selected from the group consisting of argon, nitrogen and *freon*.
>
> U.S. Pat. No. 5,988,438 - Apparatus for rapid inflation of inflatable object and related method

14. The inflator device according to claim 1, wherein the liquified gas comprises at least one of a *freon,* a halon, nitrogen, or carbon dioxide.

Therefore, the USPTO has agreed, for over twenty five years (*i.e.*, since the 1976 issuance of U.S. Pat. No. 3,938,114), that the use of the term "freon" is well understood and does not make a claim indefinite. Thus, withdrawal of this rejection is respectfully requested.

We note that several claims containing the term "freon" have been analyzed by Courts but we are not aware of any case where a claim was held indefinite because of its use of the term "freon."

3. The Use Of Generic Names Is Permissible

Additionally, generic names for chemicals are permissible for use in claims if their meanings are well-known and satisfactorily defined in the literature. The term "freon" is used not only to refer to the refrigerants sold by DuPont, but is used generally by the art to refer to a well-known family of fluorinated carbon-containing compounds which have a distinctive set of characteristics. Thus, the use of the term "freon" is permissible in claims and withdrawal of this rejection is respectfully requested.

4. There Is No Objective Evidence To Support The Rejection

The Examiner argues that the use of the term "freon" in claim 44 renders it indefinite. However, the Examiner does not, and Applicants believe, cannot show any evidence in support. The Examiner cites to Freon-11, Freon-12 and Freon-114, all of which were undeniably known as freons as of Applicants' filing date. Thus, these freons do not support the rejection. Applicants are not aware of, nor has the Examiner cited, any chemicals that one skilled in the art would not have known was a freon. Therefore, this rejection should be withdrawn because it lacks an objective basis.

Accordingly, Applicants respectfully submit that claims 34-35, 41 and 42-44 are definite under 35 U.S.C. § 112, ¶ 2. Withdrawal of this rejection is requested.

B. Double Patenting

The Examiner has rejected claims 32-36 and 39-44 over a number of Applicants' patents and pending applications, many of which claim microbubbles and microballoons, not dry microballoons as is claimed in this application. Office Action, pp. 5-7. Applicants respectfully disagree with the Examiner's position, but since this is a provisional rejection, Applicants respectfully request that this issue be held in abeyance until the pending claims have otherwise been allowed. Applicants will then offer to file a terminal disclaimer if appropriate.

C. Applicants' Dry Microballoons Are Patentable And Nonobvious Over The Cited References Under 35 U.S.C. § 103

The Examiner rejected claims 32-36 and 39-44 as being purportedly unpatentable over several cited references. Specifically, the Examiner stated that one of ordinary skill in the art would have been motivated to form the Applicants' claimed invention by:

(a) using the teachings of Ganguly to optimize the wall thickness and surface porosity of the microbubble of Feinstein or microcapsules of Temple, and further combining the teachings of Tickner to use freon gas. Office Action, pp. 8-11.

(b) using the teachings of Ganguly to optimize the wall thickness and surface porosity of the microbubble of Reinhardt, and further combining the teachings of Tickner to use freon gas. Office Action, pp. 11-13.

Applicants respectfully traverse. The references relied upon by the Examiner fail to provide the necessary incentive or motivation to combine them in an attempt to create the Applicants' claimed invention. There is nothing in any of the references to suggest the desirability of the combination or modification in the manner indicated by the Examiner. Thus,

the combination of references proposed by the Examiner is improper and Applicants respectfully request that this rejection be withdrawn.

Furthermore, even if such combination were somehow proper, no such combination would yield the Applicants' invention. Namely, no combination teaches dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid as claimed by Applicants. Thus, withdrawal of this rejection is respectfully requested.

1. There Is No Suggestion In The Cited References To Combine

It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion, or motivation to lead one of ordinary skill in the art to combine those references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617-18 (Fed.Cir. 1999)("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.")

Merely asserting that it would have been within the skill of the art to substitute one type of gas for another in the contrast agent of the primary reference is not enough. *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed.Cir. 1988)(Holding that there was no support for the Examiner's mere assertion that it would have been obvious to substitute one type of detector for another in the system of the primary reference); *In re Jones*, 21 U.S.P.Q.2d 1941 (Fed.Cir. 1992)(Holding that there was no suggestion to combine a primary herbicide reference with secondary references directed to shampoo additives or byproducts of mopholines to arrive at the claimed invention.); MPEP § 2143.01.

There is nothing in any of the cited references to suggest the desirability of the combination or modification in the manner indicated by the Examiner. Specifically, there is no motivation or suggestion to combine Feinstein, Temple, or Reinhardt with Ganguly and/or Tickner.

a. Summary Of References

i. Feinstein

Feinstein disclose microballoon structures made from, *inter alia*, denatured serum albumin. These microballoon structures entrap gas and serve as the "agent" for use with ultrasound. The reported stability of these microballoon structures is attributed to the denatured albumin wall. Feinstein, col. 4, lines 57-59. They do not dissolve in the bloodstream to release free gas microbubbles (i.e., gas bubbles with nothing surrounding the gas), nor can they be ground without destroying the structures themselves. There is also no teaching or suggestion anywhere of dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid.

ii. Temple

Temple is directed to microcapsules which are used to entrap non-solvents such as medicament, food, vitamin, mineral, biocide, insecticide, chemical reactant, curing agents, catalysts, herbicide, fungicide, mildewcide, perfumes, odorants, fertilizers, repellants, etc. Temple, col. 9, lines 1-6. Various conventional or colored pigments may also be incorporated into the microcapsules. Temple, col. 9, lines 7-20. There is no teaching or suggestion anywhere of gas filled microballoons for use with ultrasonic echography. There is also no teaching or suggestion anywhere of dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid.

iii. Reinhardt

Reinhardt is directed to a method of obtaining an ultrasonic image using a Doppler mode with certain types of microparticles. Reinhardt, col. 3, lines 28-42. Specifically, Reinhardt's method involves the use of ultrasound Doppler mode to burst the microparticle wall and allow the ultrasound to reach deeper tissues. Reinhardt, col. 3, line 66 - col. 4, line 13. There is no teaching or suggestion anywhere of dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid.

iv. Ganguly

Ganguly is directed to polystyrene microspheres for use as sensitizers in explosives. Ganguly, p. 193. Ganguly reports on a SEM study comparing polystyrene microspheres which entrap methanol vs. nitrite solution. There is no teaching or suggestion anywhere that these microspheres may be used for ultrasonic echography. There is also no teaching or suggestion anywhere that these microspheres may be gas filled. There is further no teaching or suggestion anywhere of dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid.

v. Tickner

Tickner is directed to saccharide microparticle precursors which dissolve in the bloodstream to release free gas microbubbles which reflect the ultrasound signal and serve as the contrast agent:

> It follows that a plurality of ultrasonic signals are generated as a function of time as the various microbubbles are formed on dissolving of the various particles 26 or on dissolving of portions thereof.
>
> * * *
>
> Briefly, as each microbubble is formed by dissolving of at least part of the wall 32 to expose the hollow space 30 or as the wall 32 thins sufficiently to cause the pressurized bubble 30 to fracture it,

> the microbubble expands beyond its equilibrium size, and alternately expands and contracts until it finally attains substantially its equilibrium size and shape. The frequency of the signal thereby detected by the transducer 34 is a function of the pressure in the cardiovascular system 12 opposite the positioning of the transducer 34.

Tickner, col. 4, lines 31-62. Figure 2 of Tickner illustrates the irregular reduction of the saccharide outer wall as it dissolves to release free gas microbubbles. These free gas microbubbles have no structure or envelope surrounding the gas. Additionally, Tickner recommends grinding to reduce the size and number of hollow spaces of the solid precursor microparticles. Tickner, col. 4, lines 11-14. There is no teaching or suggestion anywhere of dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid.

b. The References Are Directed To Different Inventions

There is no motivation to combine Feinstein or Temple or Reinhardt with Ganguly or Tickner in the manner suggested by the Examiner because they are directed toward completely different inventions for different applications.

For example, one of ordinary skill in the art will not be motivated to combine: (a) the non-dissolving, non-grindable contrast agent gas filled microballoons of Feinstein with (b) the liquid filled explosive sensitizer microspheres of Ganguly and/or (c) the dissolving, grindable saccharide microparticles which release the free gas microbubble contrast agent of Tickner. In other words, no skilled artisan will combine unrelated and different liquid and gas microvesicle[2] references directed to different applications. Additionally, the mere coincidence that the contrast

[2] While microparticles, microballoons, microbubbles, microcapsules, free gas microbubbles, etc. all refer to different inventions in the cited art and this application, for simplicity, Applicants will use the term "microvesicle" to refer to them collectively where convenient. This is not an admission in any way that they are the same or even remotely related.

agents disclosed in both Feinstein and Tickner are used for ultrasonic imaging does not make them combinable since they operate in a completely different manner - one relying on a microballoon structure, the other on free gas microbubbles without any structure.

Furthermore, one of ordinary skill in the art will also not be motivated to combine: (a) the household liquid nonsolvent filled microcapsules of Temple with (b) the liquid filled explosive sensitizer microspheres of Ganguly and/or (c) the dissolving, grindable saccharide microparticles which release the free gas microbubble contrast agent of Tickner. No skilled artisan will combine these unrelated and different liquid and gas microvesicle references directed to different applications.

Moreover, one of ordinary skill in the art will further not be motivated to combine: (a) Reinhardt's method to burst microparticle walls with (b) the liquid filled explosive sensitizer microspheres of Ganguly and/or (c) the dissolving, grindable saccharide microparticles which release the free gas microbubble contrast agent of Tickner. Specifically, no skilled artisan will use Reinhardt's teaching to burst explosives containing the liquid microspheres of Ganguly, or to burst the free gas microbubbles of Tickner which have no walls to burst.

With the cited references all directed to completely different inventions, there is no motivation or suggestion to combine them.

c. Feinstein Teaches Away From Modification

Furthermore, Feinstein teaches against the modification of its invention or the combination of parts of its invention with Tickner because Feinstein asserts that its agents are superior to all others, with no problems suggested or improvements needed. It is especially significant that despite the previous publication of the Tickner reference, Feinstein chose not to incorporate or adopt Tickner's teaching regarding gases. The Examiner's proposed combination thus would not have been made by one of ordinary skill in the art.

Moreover, there are no road signs or blaze marks in the references that would lead one to ignore the bulk of their teachings and recommendations and be led to anything like Applicants' specific dry microballoons.

2. The Mere Fact That References Can Be Modified Or Combined Is Not Enough

Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783-1784 (Fed. Cir. 1992)(emphasis added):

> The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification.

Thus, the mere fact that references can be combined or modified (and Applicants believe they cannot) does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed.Cir. 1990); MPEP § 2143.01. Hence, the Examiner's attempt to combine the cited references without any overall suggestion in the references of the desirability of the modification is improper and should be withdrawn.

For example, there is no overall suggestion in any of the cited combinations of why the encapsulated material should be gas as opposed to liquid. There is also no overall suggestion in any of the cited combinations of why the microvesicle at issue should be designed for ultrasonic echography instead of explosives or commercial household use, or why one microvesicle is preferred over the other (*e.g.*, free gas vs. walled, etc.) There is further no suggestion anywhere of why a freon should be the encapsulated material instead of any other preferred gases or liquids. In particular, there is no suggestion to ignore Tickner's preference for carbon dioxide or Temple's teachings for liquid materials. Since each reference suggests its own encapsulated

material and applications for use, there cannot be any overall suggestion to choose one encapsulated material, application, etc. over another.

3. The Modification Cannot Change
The Principle Of Operation Of A Reference

The proposed modification cannot change the principle of operation of a reference. *In re Ratti*, 123 U.S.P.Q. 349 (C.C.P.A. 1959); MPEP § 2143.01. However, the Examiner's proposed modification would effectively change the principle of operation of each reference. In particular, the following modifications are improper:

a) Feinstein (gas filled microspheres) cannot be combined with Ganguly (liquid filled microspheres) since the material encapsulated (gas vs. liquid) and their applications (explosives vs. ultrasound) require completely different principles of operation.

b) Feinstein (albumin microspheres) cannot be combined with Tickner (free gas microbubbles) because Feinstein explicitly relies on the benefits of an albumin shell surrounding the gas while Tickner relies on the benefits of a free gas bubble without anything surrounding the gas, a completely different principle of operation.

c) Ganguly (liquid filled microspheres) cannot be combined with Tickner (free gas microbubbles) since the materials used (liquid vs. gas; walled vs. free gas) and their applications (explosives vs. ultrasound) require completely different principles of operations.

d) Temple (commercial liquid nonsolvent filled microcapsules) cannot be combined with Ganguly (liquid filled microspheres) since their applications (commercial household use vs. explosives) require completely different principles of operation.

e) Temple (commercial liquid nonsolvent filled microcapsules) cannot be combined with Tickner (free gas microbubbles) since the materials used (liquid vs. gas; walled vs. free gas) and

their applications (commercial household use vs. ultrasound) require completely different principles of operations.

f) Reinhardt (bursting microparticles) cannot be combined with Ganguly (liquid filled microspheres) since their applications (ultrasound vs. explosives) require completely different principles of operation.

g) Reinhardt (bursting microparticles) cannot be combined with Tickner (free gas microbubbles) because Reinhardt explicitly relies on the benefits of bursting a microparticle wall while Tickner relies on the benefits of a free gas bubble without any such wall surrounding the gas, a completely different principle of operation.

Since the Examiner's proposed modification would thus improperly change the principle of operation of these references, withdrawal of this rejection is respectfully requested.

4. There Is No Reasonable Expectation Of Success

There also must be a reasonable expectation of success from the prior art in combining the references. *In re Vaeck,* 947 F.2d 488, 20 U.S.P.Q.2d 1438, 1442 (Fed.Cir. 1991). This motivation to combine and the reasonable expectation of success both must be found in the prior art and not the Applicants' disclosure. *In re Vaeck,* 20 U.S.P.Q.2d at 1442. Using the Applicant's own disclosure in an obviousness analysis is considered improper and prohibited by case law. *Grain Processing Corp. v. American Maize-Products Co.*, 840 F.2d 902, 907, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988)("Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.'"); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988)("One cannot use hindsight

reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.")

For example, since Feinstein, Tickner and Ganguly are directed to completely different types of materials (gas vs. liquid) and applications (ultrasound vs. explosives), there is no reasonable expectation of success that these references may be combined as suggested by the Examiner. Additionally, since Feinstein and Tickner are directed to vastly different types of contrast agents (one with a structure, the other without), there is also no reasonable expectation of success that Feinstein may be combined with Tickner as suggested by the Examiner.

Furthermore, since Temple, Ganguly and Tickner are directed to completely different types of materials (liquid vs. gas; walled vs. free gas) and applications (commercial household use vs. explosives vs. ultrasound), there is no reasonable expectation of success that these references may be combined as suggested by the Examiner.

Moreover, since Reinhardt, Ganguly and Tickner are directed to completely different types of materials (gas vs. liquid; walled vs. free gas) and applications (ultrasound vs. explosives), there is no reasonable expectation of success that these references may be combined with Ganguly as suggested by the Examiner. Additionally, since Reinhardt and Tickner are directed to vastly different types of contrast agents (bursting a structure vs. free gas without a structure), there is also no reasonable expectation of success that Reinhardt may be combined with Tickner as suggested by the Examiner.

Without any reasonable expectation of success, it is improper to combine the references cited by the Examiner and withdrawal of this rejection is respectfully requested.

5. The Cited Combination Still Does Not Yield Applicants' Claimed Invention

Even if the cited reference combination proposed by the Examiner were somehow proper, no such combination would yield the Applicants' invention. Namely, no combination teaches dry microballoons which form an aqueous dispersion of gas filled microballoons upon dispersion in an aqueous carrier liquid as claimed by Applicants. Thus, for this additional reason, withdrawal of this rejection is respectfully requested.

D. Conclusion

In light of the above, Applicants respectfully submit that pending claims 32-33 and 35-50 are now in condition for allowance and notice to that effect is respectfully requested.

No new matter has been added.

If there are any further points requiring attention prior to allowance, the Examiner is asked to contact Applicant's counsel.

No extra fee is required. If there are additional fees, please charge them to our firm Deposit Account No. 14-1140.

Respectfully submitted,

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EXHIBIT A

Marked Up Version of Amended Claims 35
(Additions underlined, deletions bracketed)

35. (Once Amended) The dry microballoons of claim [34] 32, wherein the polymer membrane has a porosity of 50 to 2,000 nm.

41. (Once Amended) The dry microballoons of claim 40, wherein the plasticizers include isopropyl myristate, and glyceryl monostearate [and the like] to control flexibility, the amphipatic substances include surfactants and phospholipids like the lecithins to control permeability by increasing porosity and the hydrophobic compounds are high molecular weight hydrocarbon paraffin-waxes to reduce porosity.